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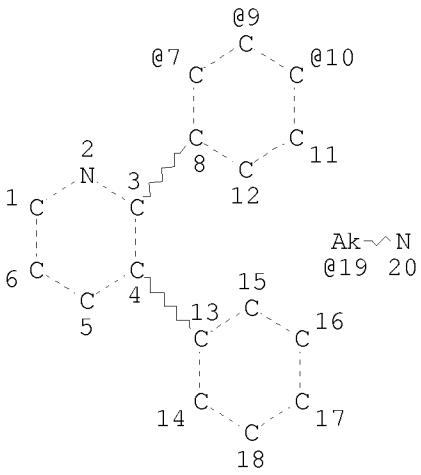


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NODE ATTRIBUTES:
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GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE


=> d his l8

     (FILE 'REGISTRY' ENTERED AT 09:33:10 ON 28 OCT 2008)
L8           565 S L6 FUL

=> d his l9

     (FILE 'CAPLUS' ENTERED AT 09:40:23 ON 28 OCT 2008)
L9            19 S L8

=> d his l10

     (FILE 'CAPLUS' ENTERED AT 09:40:23 ON 28 OCT 2008)
L10           14 S L9 AND CANCER?

=> d his l11

     (FILE 'CAPLUS' ENTERED AT 09:40:23 ON 28 OCT 2008)
L11            5 S L9 NOT L10

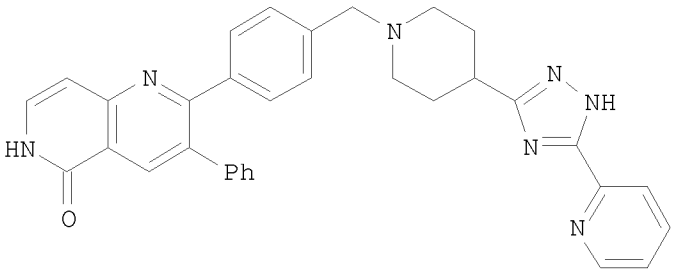
=> d bib abs 1-5

L11  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2008:874033  CAPLUS
DN   149:282463
```

TI The design and synthesis of potent and cell-active allosteric dual Akt 1 and 2 inhibitors devoid of hERG activity
AU Siu, Tony; Li, Yiwei; Nagasawa, Johnny; Liang, Jun; Tehrani, Lida; Chua, Peter; Jones, Raymond E.; Defeo-Jones, Deborah; Barnett, Stanley F.; Robinson, Ronald G.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck & Co., San Diego, CA, 92129, USA
SO Bioorganic & Medicinal Chemistry Letters (2008), 18(14), 4191-4194
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
AB This letter details the attenuation of hERG in a class of Akt inhibitors through heteroatom insertions into aromatic rings. The development of a cell-active dual Akt 1 and 2 inhibitors devoid of hERG activity is discussed using structure-activity relationships.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:874031 CAPLUS
DN 149:282462
TI Discovery of potent and cell-active allosteric dual Akt 1 and 2 inhibitors
AU Siu, Tony; Liang, Jun; Arruda, Jeannie; Li, Yiwei; Jones, Raymond E.; Defeo-Jones, Deborah; Barnett, Stanley F.; Robinson, Ronald G.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck & Co., San Diego, CA, 92129, USA
SO Bioorganic & Medicinal Chemistry Letters (2008), 18(14), 4186-4190
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
AB This paper describes the improvement of cell potency in a class of allosteric Akt 1 and 2 inhibitors. Key discoveries include identifying the solvent exposed region of the mol. and appending basic amines to enhance the physiochem. properties of the mols. Findings from the structure-activity relationships are discussed.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:668183 CAPLUS
DN 149:215065
TI Allosteric inhibitors of Akt1 and Akt2: A naphthyridinone with efficacy in an A2780 tumor xenograft model
AU Bilodeau, Mark T.; Balitza, Adrienne E.; Hoffman, Jacob M.; Manley, Peter J.; Barnett, Stanley F.; Defeo-Jones, Deborah; Haskell, Kathleen; Jones, Raymond E.; Leander, Karen; Robinson, Ronald G.; Smith, Anthony M.; Huber, Hans E.; Hartman, George D.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck & Co., West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2008), 18(11), 3178-3182
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
GI

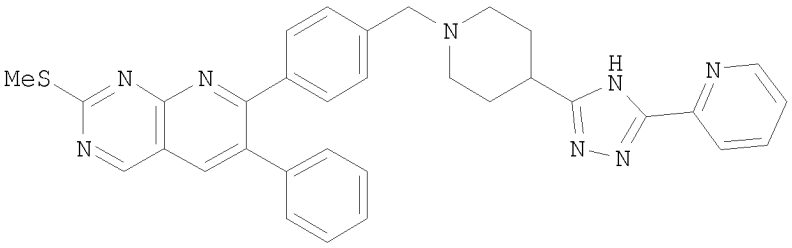


I

AB A series of naphthyridine and naphthyridinone allosteric dual inhibitors of Akt1 and 2 have been developed. These compds. have been optimized to have potent dual activity against the activated kinase as well as the activation of Akt in cells. One compound (I) has potent inhibitory activity against Akt1 and 2 in vivo in a mouse lung and efficacy in a tumor xenograft model.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:232046 CAPLUS
DN 148:449570
TI Development of pyridopyrimidines as potent Akt1/2 inhibitors
AU Wu, Zhicai; Hartnett, John C.; Neilson, Lou Anne; Robinson, Ronald G.; Fu, Sheng; Barnett, Stanley F.; Defeo-Jones, Deborah; Jones, Raymond E.; Kral, Astrid M.; Huber, Hans E.; Hartman, George D.; Bilodeau, Mark T.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck and Co., West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2008), 18(4), 1274-1279
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 148:449570
GI



I

AB This communication reports a new synthetic route of pyridopyrimidines, e.g., I, to facilitate their structural optimization in a library fashion and describes the development of pyridopyrimidines that have excellent enzymic and cell potency against Akt1 and Akt2. This series also shows a high level of selectivity over other closely related kinases and significantly improved caspase-3 activity with the more optimized compds.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:263668 CAPLUS
DN 142:482177
TI Synthesis and biological evaluation of unnatural canthine alkaloids
AU Lindsley, Craig W.; Bogusky, Michael J.; Leister, William H.; McClain, Ray T.; Robinson, Ronald G.; Barnett, Stanley F.; Defeo-Jones, Deborah; Ross, Charles W., III; Hartman, George D.
CS Department of Medicinal Chemistry, Technology, Enabled Synthesis Group, Merck Research Laboratories, Merck & Co., West Point, PA, 19486, USA
SO Tetrahedron Letters (2005), 46(16), 2779-2782
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 142:482177
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Employing a 'one-pot' microwave-assisted protocol, unnatural canthine alkaloids, e.g. I and II, with biol. activities beyond the natural products were prepared This report describes unnatural canthine alkaloid analogs as selective, allosteric Akt kinase inhibitors.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs l10 1-14

L10 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:338631 CAPLUS
DN 148:528852
TI Rapid assembly of diverse and potent allosteric Akt inhibitors
AU Wu, Zhicai; Robinson, Ronald G.; Fu, Sheng; Barnett, Stanley F.; Defeo-Jones, Deborah; Jones, Raymond E.; Kral, Astrid M.; Huber, Hans E.; Kohl, Nancy E.; Hartman, George D.; Bilodeau, Mark T.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck & Co., West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2008), 18(6), 2211-2214
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 148:528852
AB This paper describes the rapid assembly of four different classes of potent Akt inhibitors from a common intermediate. Among them, a pyridopyrimidine series displayed the best intrinsic and cell potency against Akt1 and Akt2. This series also showed a promising pharmacokinetic profile and excellent selectivity over other closely related kinases.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:338620 CAPLUS
DN 148:552728
TI Optimization of 2,3,5-trisubstituted pyridine derivatives as potent allosteric Akt1 and Akt2 inhibitors

AU Hartnett, John C.; Barnett, Stanley F.; Bilodeau, Mark T.; Defeo-Jones, Deborah; Hartman, George D.; Huber, Hans E.; Jones, Raymond E.; Kral, Astrid M.; Robinson, Ronald G.; Wu, Zhicai
CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck & Co., West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2008), 18(6), 2194-2197
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 148:552728
AB This letter shows inhibitor SAR on a pyridine series of allosteric Akt inhibitors to optimize enzymic and cellular potency. We have optimized 2,3,5-trisubstituted pyridines to give potent Akt1 and Akt2 inhibitors in both enzyme and cell based assays. In addition, we will also highlight the pharmacokinetic profile of an optimized inhibitor that has low clearance and long half-life in dogs.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:1060852 CAPLUS
DN 147:378396
TI nf-kb activation inhibitors for treating muscular wasting diseases
IN Guttridge, Denis C.; Baldwin, Albert S.
PA Theralogics, Inc., USA
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007106884	A2	20070920	WO 2007-US64057	20070315
	WO 2007106884	A3	20080529		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	US 20070225315	A1	20070927	US 2007-686623	20070315
PRAI	US 2006-782427P	P	20060315		

AB Methods for treating muscular wasting diseases such as Duchenne muscular dystrophy are disclosed. Specifically, the methods include administering to a subject in need of treatment a nuclear factor kappa B (NF-KB) activation inhibitor capable of blocking the activation of NF-KB. Administration of peptides comprised of a Nuclear Factor Essential (NEMO) binding domain to a mouse model of Duchenne muscular dystrophy significantly increased diaphragm contractions.

L10 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1338025 CAPLUS
DN 146:100699
TI Naphthyridine compounds as Akt inhibitors and their preparation,

pharmaceutical compositions, and use in the treatment of cancer

IN Armstrong, Donna J.; Hu, Essa H.; Kelly, Michael J., III; Layton, Mark E.; Li, Yiwei; Liang, Jun; Rodzinak, Kevin J.; Rossi, Michael A.; Sanderson, Philip E.; Wang, Jiabing

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 199pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006135627	A2	20061221	WO 2006-US22079	20060607
	WO 2006135627	A3	20080731		
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	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	AU 2006258124	A1	20061221	AU 2006-258124	20060607
	CA 2610888	A1	20061221	CA 2006-2610888	20060607
	EP 1898903	A2	20080319	EP 2006-772406	20060607
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	MX 200715578	A	20080306	MX 2007-15578	20071207
	KR 2008016627	A	20080221	KR 2007-728878	20071210
	IN 2007DN10098	A	20080620	IN 2007-DN10098	20071227
	NO 2008000150	A	20080310	NO 2008-150	20080109
PRAI	US 2005-689726P	P	20050610		
	US 2005-734188P	P	20051107		
	WO 2006-US22079	W	20060607		

OS MARPAT 146:100699

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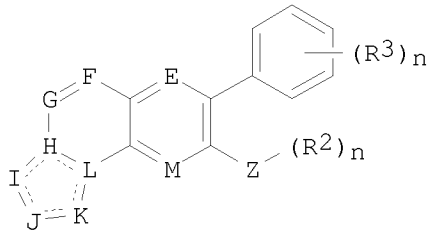

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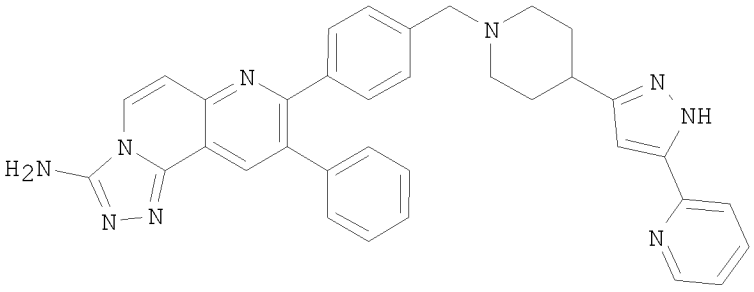

II

AB The invention provides for substituted naphthyridine compds. of formula I that inhibit Akt activity. Compds. of formula I wherein E, F, G, H, I, J, K, L and M are independently (un)substituted C and N; n is 0, 1, 2, 3, 4, and 5; each R2 and R3 are independently oxo, acyl, carbonyloxyalkyl, alkyl, carbonyloxyaryl, aryl, CO2H and derivs., halo, OH, etc.; Z is C3-8 cycloalkyl, (hetero)aryl, and heterocyclyl; and a pharmaceutically acceptable salts and stereoisomers thereof, are claimed. In particular, the compds. disclosed selectively inhibit one or two of the Akt isoforms. The invention also provides for compns. comprising such inhibitory compds. and methods of inhibiting Akt activity by administering the compound to a patient in need of treatment of cancer. Example compound II was prepared by chlorination of 3-phenyl-2-(4-[[-5-pyridin-2-yl-1H-1,2,4-triazol-3-yl)piperidin-1-yl]methyl]phenyl-1,6-naphthyridin-5(6H)-one; The resulting 5-chloro-3-phenyl-2-(4-[[-5-pyridin-2-yl-1H-1,2,4-triazol-3-yl)piperidin-1-yl]methyl]phenyl-1,6-naphthyridine underwent hydrazination to give 5-hydrazino-3-phenyl-2-(4-[[-5-pyridin-2-yl-1H-1,2,4-triazol-3-yl)piperidin-1-yl]methyl]phenyl-1,6-naphthyridine, which underwent cyclization with 1,1'-diimidazol-1-ylmethanamine to give compound II. All the invention compds. were evaluated for their Akt inhibitory activity.

L10 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1095230 CAPLUS
DN 145:454994
TI Preparation of naphthyridines as inhibitors of Akt kinase activity for treating cancer
IN Chen, Chixu; Eastman, Brian W.; Hu, Essa H.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 58pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006110638	A2	20061019	WO 2006-US13280	20060410
	WO 2006110638	A3	20070419		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

AU	2006235314	A1	20061019	AU 2006-235314	20060410
CA	2602197	A1	20061019	CA 2006-2602197	20060410
EP	1871376	A2	20080102	EP 2006-749636	20060410
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP	2008535915	T	20080904	JP 2008-506570	20060410
CN	101155588	A	20080402	CN 2006-80011545	20071009
IN	2007DN07768	A	20071109	IN 2007-DN7768	20071010
PRAI US	2005-670469P	P	20050412		
	WO 2006-US13280	W	20060410		

OS MARPAT 145:454994

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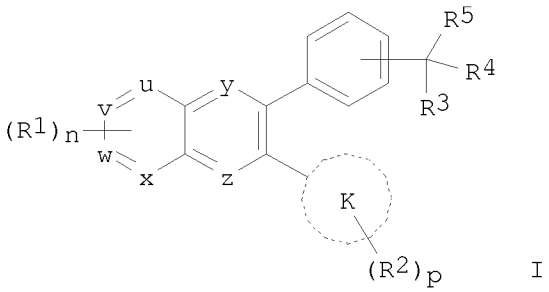

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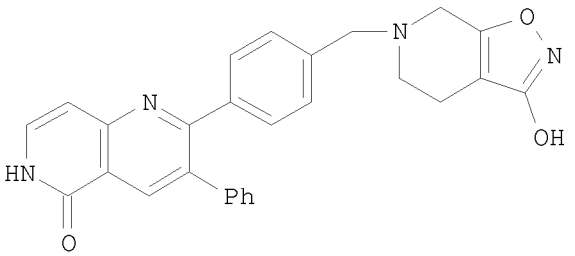

II

AB The instant invention provides for compds. of general formula I (wherein n = 0-4; p = 0-5; u, v, w, x, y, and z = CH and N; Ring K = (C3-C8)cycloalkyl, aryl, heteroaryl and heterocyclyl; R1 and R2 = oxo, carbonyl alkoxy, carbonyl aryloxy, etc.; R3 and R4 = H, (C1-C6)alkyl, (C1-C6)perfluoroalkyl, etc.; R5 = substituted amino; R6 = carbonyl alkoxy, C2-C10 alkenyl, etc.) that inhibit Akt activity. In particular, the compds. disclosed selectively inhibit one or two of the Akt isoforms. The invention also provides for compns. comprising such inhibitory compds. and methods of inhibiting Akt activity by administering the compound to a patient in need of treatment of cancer. Preparation of I is

exemplified. For example, II was prepared in 5 steps from an initial reaction between tert-Bu (2-chloro-3-formylpyridin-4-yl)carbamate and 1-[4-(1,3-Dioxolan-2-yl)phenyl]-2-phenylethanone. In Akt kinase assays, the example compds. had IC50 values ≤ 50 μM against one or more of Akt1, Akt2, and Akt3. Also exemplified in the patent is cloning of human Akt isoforms and ΔPH-Akt1.

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:634244 CAPLUS
DN 145:96419
TI Canthine analog inhibitors of Akt kinase activity, and use in the treatment of cancer
IN Barnett, Stanley F.; Bogusky, Michael J.; Leister, William H.; Lindsley, Craig W.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006068796	A2	20060629	WO 2005-US43361	20051128
	WO 2006068796	A3	20061207		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2005319606	A1	20060629	AU 2005-319606	20051128
	CA 2588474	A1	20060629	CA 2005-2588474	20051128
	EP 1824849	A2	20070829	EP 2005-857040	20051128
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 101068811	A	20071107	CN 2005-80041367	20051128
	JP 2008521917	T	20080626	JP 2007-544476	20051128
	US 20080015212	A1	20080117	US 2007-791418	20070523
	IN 2007DN04186	A	20070831	IN 2007-DN4186	20070601
PRAI	US 2004-632490P	P	20041202		
	WO 2005-US43361	W	20051128		

OS CASREACT 145:96419; MARPAT 145:96419
AB The invention provides canthine analogs that inhibit Akt activity. In particular, the compds. disclosed selectively inhibit one or two of the Akt isoforms. The invention also provides for compns. comprising such inhibitory compds. and methods of inhibiting Akt activity by administering the compound to a patient in need of treatment of cancer. Compound preparation is included.

L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:608573 CAPLUS
DN 145:103647
TI Preparation of naphthyridine derivatives as inhibitors of Akt activity
IN Arruda, Jeannie M.; Campbell, Brian T.; Cosford, Nicholas D. P.; Hoffman, Jacob M.; Hu, Essa H.; Layton, Mark E.; Li, Yiwei; Liang, Jun; Rodzinak,

Kevin J.; Siu, Tony; Stearns, Brian A.; Tehrani, Lida R.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006065601	A2	20061019	WO 2005-US44294	20051209
	WO 2006065601	A3	20070809		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	AU 2005316826	A1	20060622	AU 2005-316826	20051209
	CA 2589084	A1	20060622	CA 2005-2589084	20051209
	EP 1827436	A2	20070905	EP 2005-853256	20051209
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	JP 2008524339	T	20080710	JP 2007-556133	20051209
	IN 2007DN04504	A	20070831	IN 2007-DN4504	20070613
	CN 101242834	A	20080813	CN 2005-80043064	20070614
PRAI	US 2004-636203P	P	20041215		
	WO 2005-US44294	W	20051209		

OS MARPAT 145:103647

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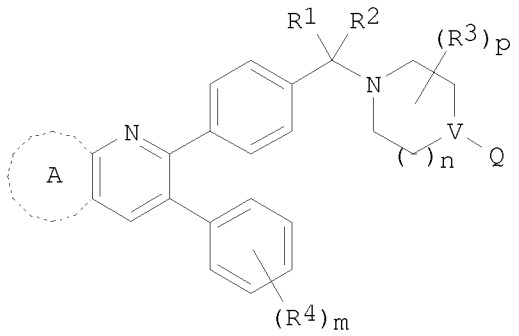

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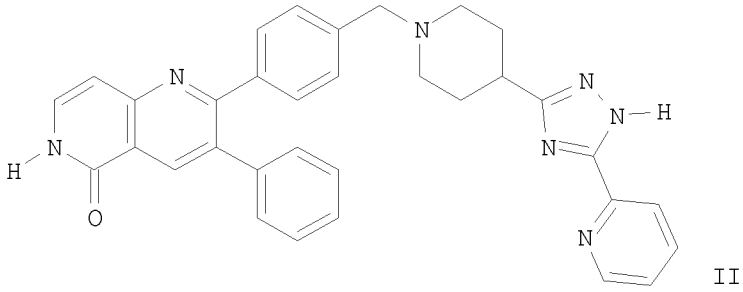


II

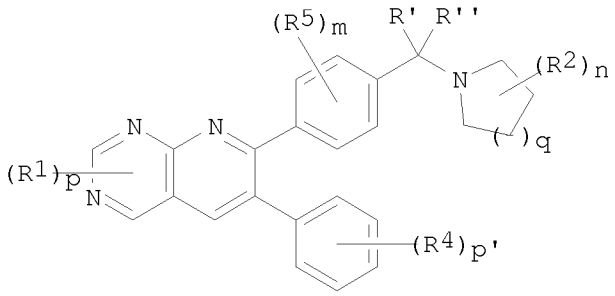
AB Title compds. I [Ring A forms a fused substituted 6-membered ring containing N; R1 and R2 independently = H, alkyl, perfluoroalkyl or combined to form a carbocycle or heterocycle; R3 independently = halo, alkyl, hydroxyalkyl, etc.; R4 independently = halo, oxo, OH , CN, etc.; m = 0-4; n = 0-1; p = 0-4; Q = aryl, arylcarbonyl, heterocycle, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as having the ability to inhibit the activity of Akt, a serine/threonine protein kinase. Thus, e.g., II was prepared via reductive amination of 4-(5-methoxy-3-phenyl-1,6-naphthyridin-2-yl)benzaldehyde (preparation given) with 2-(3-piperidin-4-yl-1H-1,2,4-triazol-5-yl)pyridine dihydrochloride (preparation given) followed by demethylation. In described assays for Akt kinase inhibition, specific compds. of the invention were tested and found to have IC50 values of ≤ 50 μM against one or more of Akt1, Akt2 and Akt3. The invention is further directed to chemotherapeutic compns. containing the compds. of this invention and methods for treating cancer comprising administration of the compds. of the invention. These substituted naphthyridines have unexpected advantageous properties when compared to other naphthyridines reported in PCT publication WO2003/086394, such unexpected advantageous properties may include increased cellular potency/solubility, greater selectivity, enhanced pharmacokinetic properties, lack of off target activity, etc.

L10 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:318893 CAPLUS
DN 144:370118
TI Preparation of pyrido[2,3-d]pyrimidine derivatives as inhibitors of Akt activity for treatment of cancer
IN Bilodeau, Mark T.; Cosford, Nicholas D. P.; Hartnett, John C.; Liang, Jun; Manley, Peter J.; Neilson, Lou Anne; Siu, Tony; Wu, Zhicai; Li, Yiwei
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006036395	A2	20060406	WO 2005-US29941	20050819
	WO 2006036395	A3	20071221		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	AU 2005290081	A1	20060406	AU 2005-290081	20050819
	CA 2576172	A1	20060406	CA 2005-2576172	20050819
	EP 1784175	A2	20070516	EP 2005-807835	20050819
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	JP 2008510823	T	20080410	JP 2007-530047	20050819
	US 20070254901	A1	20071101	US 2007-659606	20070206
	CN 101217958	A	20080709	CN 2005-80028144	20070216
	IN 2007DN02189	A	20070803	IN 2007-DN2189	20070321
PRAI	US 2004-603728P	P	20040823		
	WO 2005-US29941	W	20050819		

OS CASREACT 144:370118; MARPAT 144:370118

GI



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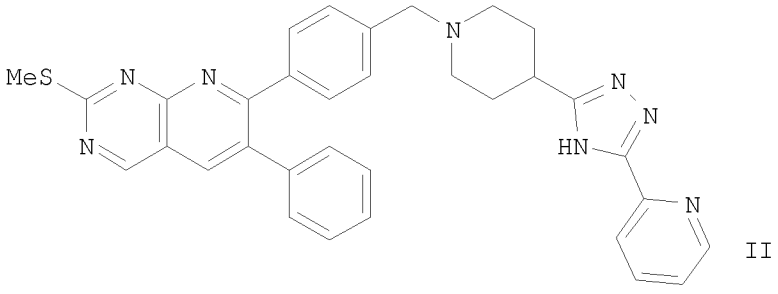

II

AB The title compds. I [wherein m = 0-4; n = 0-5; p = 0-3; q = 0-4; p' = 0-5; R1 = halo, oxo, OH, CN, etc.; R2, R4, and R5 = independently CN, CF3, NO2,

etc.; R' and R'' = independently H, alkyl, or perfluoroalkyl; or R' and R'' form a ring; with provisos] or pharmaceutically acceptable salts or stereoisomers thereof were prepared as inhibitors of the activity of Akt, which is a serine/threonine protein kinase. For example, the compound II was prepared in a multi-step synthesis. I are useful for the treatment of cancer (no data).

L10 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:86368 CAPLUS
DN 142:211437
TI Discovery of 2,3,5-trisubstituted pyridine derivatives as potent Akt1 and Akt2 dual inhibitors
AU Zhao, Zhijian; Leister, William H.; Robinson, Ronald G.; Barnett, Stanley F.; Defeo-Jones, Deborah; Jones, Raymond E.; Hartman, George D.; Huff, Joel R.; Huber, Hans E.; Duggan, Mark E.; Lindsley, Craig W.
CS Department of Medicinal Chemistry, Technology Enabled Synthesis Group, Merck Research Laboratories, Merck & Co., West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(4), 905-909
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 142:211437
AB This letter describes the discovery of a novel series of dual Akt1/Akt2 kinase inhibitors, based on a 2,3,5-trisubstituted pyridine scaffold. Compds. from this series, which contain a 5-tetrazolyl moiety, exhibit more potent inhibition of Akt2 than Akt1.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:964997 CAPLUS
DN 141:410816
TI Preparation of azaheterocyclyl-substituted diphenylpyridines as Akt inhibitors for the treatment of cancer
IN Bilodeau, Mark T.; Duggan, Mark E.; Hartnett, John C.; Lindsley, Craig W.; Wu, Zhicai; Zhao, Zhijian
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004096131	A2	20041111	WO 2004-US12188	20040420
WO 2004096131	A3	20051103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004233828	A1	20041111	AU 2004-233828	20040420
CA 2522431	A1	20041111	CA 2004-2522431	20040420
EP 1622616	A2	20060208	EP 2004-760294	20040420

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

	CN 1809354	A	20060726	CN 2004-80017118	20040420
	JP 2006524696	T	20061102	JP 2006-513160	20040420
	US 20070043001	A1	20070222	US 2005-554001	20051021
	IN 2005DN05182	A	20071019	IN 2005-DN5182	20051110
PRAI	US 2003-465260P	P	20030424		
	WO 2004-US12188	W	20040420		

OS MARPAT 141:410816

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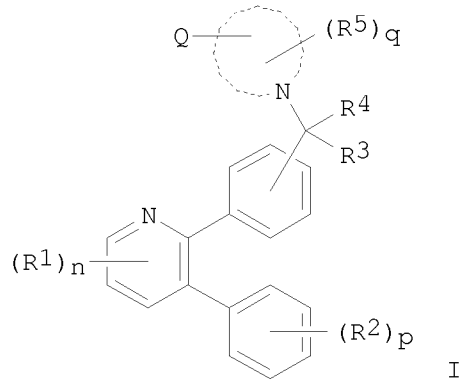

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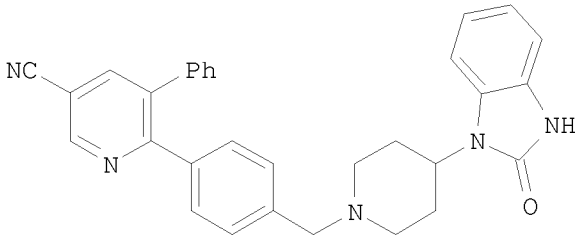

II

AB Azaheterocyclyl-substituted diphenylpyridines I [uppermost nitrogen-containing ring is a heterocycle; R1, R2, R5 = (un)substituted alkyl, aryl, heteroaryl, alkenyl, alkynyl, HO2C, NC, halo, HO, OHC, O2N, alkoxy, etc.; R3, R4 = H, alkyl, perfluoroalkyl; R3, R4, and the carbon to which they are bonded may form a carbocycle or a heterocycle containing O, S, S(:O), SO2, (un)substituted N or NHC(:O); n = 0-3; p = 0-2; q = 0-3] such as II are prepared as inhibitors of Akt1, Akt2, or Akt3 for the treatment of cancer alone or in conjunction with other drugs or radiation therapy. Trifluorosulfonylation of 6-hydroxy-5-phenyl-3-pyridinecarbonitrile, palladium-catalyzed Suzuki coupling with 4-formylphenylboronic acid, and reductive amination of the aldehyde with 1-(4-piperidinyl)-2,3-dihydro-2-benzimidazolone yields II as its TFA salt. I inhibit one or more of Akt1, Akt2, or Akt3 with IC50 values of ≤ 50 μM (no data).

L10 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:964996 CAPLUS

DN 141:406037

TI Heterocyclic compound inhibitors of Akt kinase activity, and use for the treatment of cancer

IN Bilodeau, Mark T.; Wu, Zhicai

PA Merck & Co., Inc., USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004096130	A2	20041111	WO 2004-US12187	20040420
	WO 2004096130	A3	20050407		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004233827	A1	20041111	AU 2004-233827	20040420
	CA 2522430	A1	20041111	CA 2004-2522430	20040420
	EP 1620095	A2	20060201	EP 2004-760293	20040420
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	CN 1809351	A	20060726	CN 2004-80017101	20040420
	JP 2006524254	T	20061026	JP 2006-513159	20040420
	US 20060205765	A1	20060914	US 2005-554185	20051021
PRAI	US 2003-465123P	P	20030424		
	WO 2004-US12187	W	20040420		

OS MARPAT 141:406037
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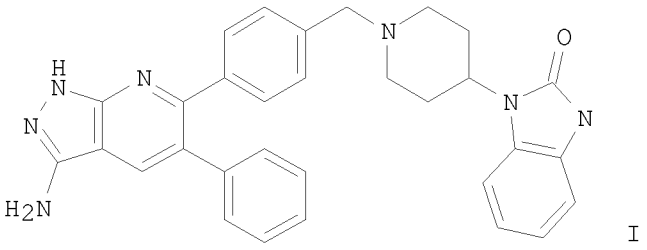

I

AB The invention discloses compds. which contain a five-membered heterocyclic ring fused to a substituted pyridine moiety which inhibit the activity of Akt, a serine/threonine protein kinase. The invention further discloses chemotherapeutic compns. containing the compds. of the invention and methods for treating cancer comprising administration of the compds. of the invention. Preparation of compds., e.g. I, is described.

L10 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:433750 CAPLUS
DN 141:7131
TI Preparation of quinazolines and analogs as Akt inhibitors and indoles as protein kinase inhibitors for use in synergistic combination therapy for

the treatment of cancer
IN Barnett, Stanley F.; Defeo-Jones, Deborah D.; Hartman, George D.; Huber, Hans E.; Stirdivant, Steven M.; Heimbrook, David C.
PA USA
SO U.S. Pat. Appl. Publ., 121 pp., which
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 20040102360	A1	20040527	US 2003-678565	20031003
PRAI US 2002-422312P	P	20021030		
US 2003-460911P	P	20030407		

OS MARPAT 141:7131
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to methods of treating cancer using a combination of at least two Akt inhibitors I [wherein Q = (un)substituted heterocyclyl, aryl; U, V, W, and X = independently CH, N; Y, Z = independently CH, N, provided that at least one of Y and Z = N; n = 0-3; p = 0-2; q = 0-4; R1, R2, R7 = independently halo, CN, OH, CHO, NO2, or (un)substituted (cyclo)alkyl(oxy), alkenyl(oxy), alkynyl(oxy), heterocyclyl(oxy), acyl, carboxy, carbamoyl(oxy), ureido, sulfamoyl, etc.; R3, R4 = independently H, (perfluoro)alkyl; or CR3R4 = cycloalkyl, heterocyclyl; and pharmaceutically acceptable salts or stereoisomers thereof] or a combination of I and a protein kinase inhibitor II [wherein G = H2, O; X = C, N, SO0-2, O; m = 0-2; n = 0-2; p = 0-6; q = 0-4; R1 = independently H, halo, or (un)substituted (cyclo)alkyl, heterocyclyl, aryl, carbamoyl, amino, acyl, sulfamoyl, carboxy, etc.; R2 = H or (un)substituted (cyclo)alkyl(oxy), amino, aryloxy, heterocyclyloxy, alkenyloxy, alkynyloxy, etc.; R5 = independently H, halo, NO2, CN, or (un)substituted alkyl, alkenyl, alkynyl, carboxy, acyl, sulfamoyl, carbamoyl, ureido, amino, etc.; and pharmaceutically acceptable salts or stereoisomers thereof], optionally in combination with a third compound Examples include syntheses for I and II and assays demonstrating Akt inhibitor activity, antitumor activity, and the synergistic effect of combinations of AKT inhibitors and/or protein kinase inhibitors on caspase 3 activity. For instance, III•HCl was prepared in an 8-step reaction sequence culminating with the cycloaddn. of 4-(2-aminoprop-2-yl)benzil and o-phenylenediamine using glacial acetic acid in H2O, followed by work up with chloroform and ethanolic HCl. III•HCl, a selective Akt1 and Akt2 inhibitor, demonstrated a 3.2-fold in caspase 3 activation over control compared to a 1.2-fold increase for a protein kinase inhibitor. Combination treatment produced a 9-fold increase in caspase 3 activation.

L10 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:836848 CAPLUS
DN 139:350754
TI Preparation of 2,3-diphenylquinoxaline derivatives as inhibitors of Akt activity for treating cancer
IN Bilodeau, Mark T.; Duggan, Mark E.; Hartnett, John C.; Lindsley, Craig W.; Manley, Peter J.; Wu, Zhicai; Zhao, Zhijian
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 228 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086394	A1	20031023	WO 2003-US10442	20030404
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2480800	A1	20031023	CA 2003-2480800	20030404
	CA 2480800	C	20080923		
	AU 2003223467	A1	20031027	AU 2003-223467	20030404
	AU 2003223467	B2	20071004		
	EP 1496896	A1	20050119	EP 2003-719597	20030404
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005533010	T	20051104	JP 2003-583413	20030404
	US 20050222155	A1	20051006	US 2004-510069	20041004
	US 7223738	B2	20070529		
PRAI	US 2002-370847P	P	20020408		
	US 2002-417174P	P	20021009		
	WO 2003-US10442	W	20030404		

OS MARPAT 139:350754
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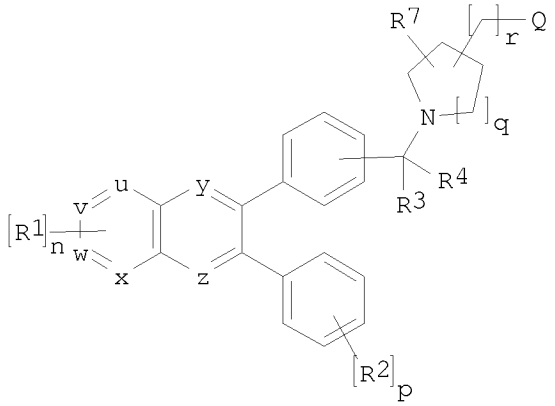

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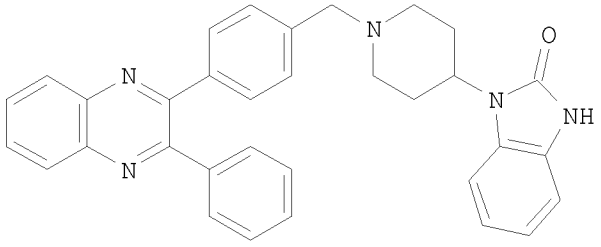

II

AB The title compds. comprising a 2,3-diphenylquinoxaline moiety [I; u, v, w and x = CH, N; y, z = CH, N (provided that at least one of y and z = N); Q = NR5R6, (un)substituted aryl, heterocyclyl; R1 = alkenyl, halo, CN, etc.; R2 = OH, CN, CO2H, etc.; R3, R4 = H, alkyl, perfluoroalkyl; or R3 and R4 are combined to form (CH2)t wherein one of the carbon atoms is optionally replaced by O, SOm, (un)substituted NHCO, N(COH); R5, R6 = H, aryl, heterocyclyl, etc.; or NR5R6 = monocyclic or bicyclic heterocycle; R7 = halo, CN, CO2H, etc.; n = 0-3; p = 0-2; t = 2-6; m = 0-2; q = 0-4; r = 0-1] and their salts which inhibit the activity of Akt, a serine/threonine protein kinase, were prepared E.g., a 2-step synthesis of the quinoxaline II [starting from 4-bromomethylbenzil and 4-(2-keto-1-benzimidazolinyl)piperidine], was given. The exemplified compds. I were found to have IC50 of ≤ 50 μM against one or more of Akt1, Akt2 and Akt3. The invention is further directed to chemotherapeutic compns. containing the compds. I and methods for treating cancer comprising administration of the compds. I.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:818232 CAPLUS
DN 139:323527
TI Preparation of triazolo[4,3-b]pyridazines and 2,3-diarylquinazolines for the treatment of cancer
IN Barnett, Stanley F.; Defeo-Jones, Deborah; Haskell, Kathleen M.; Huber, Hans E.; Nahas, Deborah D.; Lindsley, Craig W.; Zhao, Zhijian; Hartman, George D.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003084473	A2	20031016	WO 2003-US10632	20030404
	WO 2003084473	A3	20040212		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003226301	A1	20031020	AU 2003-226301	20030404
	US 20060142178	A1	20060629	US 2004-510068	20041004
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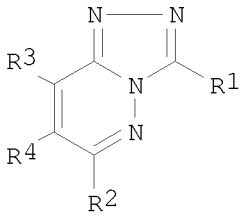
	US 2002-417202P	P	20021009		
	WO 2003-US10632	W	20030404		

GI



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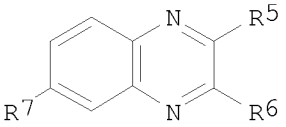

II

AB Triazolo[4,3-b]pyridazines I [R1 = (un)substituted Ph, furyl, thienyl, pyridinyl; R2 = substituted NH2, OH; R3 = H, R4 = (un)substituted cycloalkyl, aryl; R3R4 = (un)substituted CH:CHCH:CH] and quinazolines II [R5, R6 = (un)substituted Ph; R7 = H, alkyl, halogen, OH, alkoxy] were prepared for use as inhibitors of one or two of the isoforms of Akt, a serine/threonine protein kinase, acting particularly on the pleckstrin homol. domain of Akt. Thus, 3,6-dichloropyridazine was converted to its 4-cyclobutyl derivative which was cyclized with BzNHNH2 and aminated to give I [R1 = Ph, R2 = NHCH2CMe2CH2NMe2, R3 = H, R4 = cyclobutyl]. This compound had IC50 for inhibition of Akt1 of 1.4 μM.